

## CLAIMS

We claim:

1. A set of reporter signals comprising a plurality of reporter signals, wherein the reporter signals have a common property, wherein the common property allows the reporter signals to be distinguished or separated from molecules lacking the common property, wherein the reporter signals can be altered, wherein the altered forms of each reporter signal can be distinguished from every other altered form of reporter signal.
2. The set of claim 1 wherein the common property is mass-to-charge ratio, wherein the reporter signals are altered by altering their mass, wherein the altered forms of the reporter signals can be distinguished via differences in the mass-to-charge ratio of the altered forms of reporter signals.
3. The set of claim 2 wherein the mass of the reporter signals is altered by fragmentation.
4. The set of claim 2 wherein alteration of the reporter signals also alters their charge.
5. The set of claim 1 wherein the common property is mass-to-charge ratio, wherein the reporter signals are altered by altering their charge, wherein the altered forms of the labeled proteins can be distinguished via differences in the mass-to-charge ratio of the altered forms of reporter signals.
6. The set of claim 1 wherein the set comprises two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, nine or more, ten or more, twenty or more, thirty or more, forty or more, fifty or more, sixty or more, seventy or more, eighty or more, ninety or more, or one hundred or more different reporter signals.
7. The set of claim 6 wherein the set comprises ten or more different reporter signals.
8. The set of claim 1 wherein the reporter signals are peptides, oligonucleotides, carbohydrates, polymers, oligopeptides, or peptide nucleic acids.
9. The set of claim 1 wherein the reporter signals are associated with, or coupled to, specific binding molecules, wherein each reporter signal is associated with, or coupled to, a different specific binding molecule.

10. The set of claim 1 wherein the reporter signals are associated with, or coupled to, decoding tags, wherein each reporter signal is associated with, or coupled to, a different decoding tag.

11. The set of claim 1 wherein the reporter signals comprise peptides, wherein the peptides have the same mass-to-charge ratio.

12. The set of claim 11 wherein the peptides have the same amino acid composition.

13. The set of claim 12 wherein the peptides have the same amino acid sequence.

14. The set of claim 13 wherein each peptide contains a different distribution of heavy isotopes.

15. The set of claim 13 wherein each reporter signal peptide contains a different distribution of substituent groups.

16. The set of claim 12 wherein each peptide has a different amino acid sequence.

17. The set of claim 12 wherein each peptide has a labile or scissile bond in a different location.

18. The set of claim 1 wherein the reporter signals are coupled to the proteins or peptides.

19. The set of claim 1 wherein the common property allows the labeled proteins to be distinguished or separated from molecules lacking the common property.

20. The set of claim 1 wherein the common property is not an affinity tag.

21. The set of claim 20 wherein one or more affinity tags are associated with the reporter signals.

22. A method comprising

(a) separating a set of reporter signals, where each reporter signal has a common property, from molecules lacking the common property,

(b) altering the reporter signals,

(c) detecting and distinguishing the altered forms the reporter signals from each other.

23. The method of claim 22 wherein the common property is mass-to-charge ratio, wherein the reporter signals are altered by altering their mass, wherein the altered

forms of the reporter signals are distinguished via differences in the mass-to-charge ratio of the altered forms of reporter signals.

24. The method of claim 23 wherein the mass of the reporter signals is altered by fragmentation.

25. The method of claim 23 wherein the reporter signals are altered by cleavage at a photocleavable amino acid.

26. The method of claim 23 wherein the reporter signals are fragmented in a collision cell.

27. The method of claim 23 wherein the reporter signals are fragmented at an asparagine-proline bond.

28. The method of claim 23 wherein alteration of the reporter signals also alters their charge.

29. The method of claim 22 wherein the common property is mass-to-charge ratio, wherein the reporter signals are altered by altering their charge, wherein the altered forms of the labeled proteins can be distinguished via differences in the mass-to-charge ratio of the altered forms of reporter signals.

30. The method of claim 22 wherein the set of reporter signals comprises two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, nine or more, ten or more, twenty or more, thirty or more, forty or more, fifty or more, sixty or more, seventy or more, eighty or more, ninety or more, or one hundred or more different reporter signals.

31. The method of claim 30 wherein the set of reporter signals comprises ten or more different reporter signals.

32. The method of claim 22 wherein the reporter signals are peptides, oligonucleotides, carbohydrates, polymers, oligopeptides, or peptide nucleic acids.

33. The method of claim 22 wherein the reporter signals are associated with, or coupled to, specific binding molecules, wherein each reporter signal is associated with, or coupled to, a different specific binding molecule.

34. The method of claim 22 wherein the reporter signals are associated with, or coupled to, decoding tags, wherein each reporter signal is associated with, or coupled to, a different decoding tag.

35. The method of claim 22 wherein the reporter signals comprise peptides, wherein the peptides have the same mass-to-charge ratio.

36. The method of claim 35 wherein the peptides have the same amino acid composition.

37. The method of claim 36 wherein the peptides have the same amino acid sequence.

38. The method of claim 37 wherein each peptide contains a different distribution of heavy isotopes.

39. The method of claim 37 wherein each reporter signal peptide contains a different distribution of substituent groups.

40. The method of claim 36 wherein each peptide has a different amino acid sequence.

41. The method of claim 36 wherein each peptide has a labile or scissile bond in a different location.

42. The method of claim 22 wherein the reporter signals are coupled to the proteins or peptides.

43. The method of claim 22 wherein the common property allows the labeled proteins to be distinguished or separated from molecules lacking the common property.

44. The method of claim 22 wherein the common property is not an affinity tag.

45. The method of claim 44 wherein one or more affinity tags are associated with the reporter signals.

46. The method of claim 22 further comprising, prior to step (a), associating the reporter signals with one or more analytes, wherein each reporter signal is associated with, or coupled to, a different specific binding molecule, wherein each specific binding molecule can interact specifically with a different one of the analytes, wherein the reporter signals are associated with the analytes via interaction of the specific binding molecules with the analytes.

47. The method of claim 22 further comprising, prior to step (a), associating one or more reporter signals with one or more proteins, one or more peptides, or one or more proteins and peptides from each of one or more samples.

48. The method of claim 22 wherein the reporter signals are associated with a single sample.

49. The method of claim 48 wherein the sample is produced by a separation procedure, wherein the separation procedure comprises liquid chromatography, gel electrophoresis, two-dimensional chromatography, two-dimensional gel electrophoresis, isoelectric focusing, thin layer chromatography, centrifugation, filtration, ion chromatography, immunoaffinity chromatography, membrane separation, or a combination of these.

50. The method of claim 22 wherein steps (a) through (c) are repeated one or more times using a different set of reporter signals each time.

51. The method of claim 50 wherein, prior to step (a), the different sets of reporter signals are associated with different samples.

52. The method of claim 51 wherein the different sets of reporter signals each comprise the same reporter signals.

53. The method of claim 51 wherein the samples are produced by a separation procedure, wherein the separation procedure comprises liquid chromatography, gel electrophoresis, two-dimensional chromatography, two-dimensional gel electrophoresis, isoelectric focusing, thin layer chromatography, centrifugation, filtration, ion chromatography, immunoaffinity chromatography, membrane separation, or a combination of these.

54. The method of claim 51 wherein the different samples are from the same protein sample.

55. The method of claim 54 wherein the different samples are obtained at different times.

56. The method of claim 51 wherein the different samples are from the same type of organism.

57. The method of claim 51 wherein the different samples are from the same type of tissue.

58. The method of claim 51 wherein the different samples are from the same organism.

59. The method of claim 58 wherein the different samples are obtained at different times.

60. The method of claim 51 wherein the different samples are from different organisms.

61. The method of claim 51 wherein the different samples are from different types of tissues.

62. The method of claim 51 wherein the different samples are from different species of organisms.

63. The method of claim 51 wherein the different samples are from different strains of organisms.

64. The method of claim 51 wherein the different samples are from different cellular compartments.

65. The method of claim 51 further comprising identifying or preparing proteins or peptides corresponding the proteins or peptides present in one sample but not present in another sample.

66. The method of claim 51 further comprising determining the relative amount of proteins or peptides in the different samples.

67. The method of claim 50 wherein the sets of reporter signals each contain a single reporter signal.

68. The method of claim 22 wherein not all of the reporter signals in the set are distinguished or separated from molecules lacking the common property, not all of the reporter signals are altered, and not all of the altered forms of the reporter signals are detected at the same time.

69. The method of claim 68 wherein all of the reporter signals in the set are distinguished or separated from molecules lacking the common property, all of the reporter signals are altered, and all of the altered forms of the reporter signals are detected at different times.

70. The method of claim 22 wherein steps (a) through (c) are performed separately for each reporter signal.

71. The method of claim 22 wherein the altered forms of the labeled proteins detected collectively constitutes a catalog of proteins.

72. The method of claim 22 wherein steps (b) and (c) are performed simultaneously.

73. The method of claim 22 wherein the altered forms of the target protein fragments are detecting using mass spectrometry.

74. The method of claim 73 wherein the steps are performed with a tandem mass spectrometer.

75. The method of claim 74 wherein the tandem mass spectrometer comprises a first stage and a last stage, wherein step (a) is performed using the first stage of the tandem mass spectrometer to select ions in a narrow mass-to-charge range, wherein step (b) is performed by collision with a gas, and wherein step (c) is performed using the final stage of the tandem mass spectrometer.

76. The method of claim 75 where the first stage of the tandem mass spectrometer is a quadrupole mass filter.

77. The method of claim 76 where the final stage of the tandem mass spectrometer is a time of flight analyzer.

78. The method of claim 75 where the final stage of the tandem mass spectrometer is a time of flight analyzer.

79. The method of claim 74 wherein the mass-to-charge range is varied to cover the mass-to-charge ratio of each of the target protein fragments.

80. A kit comprising

(a) a set of reporter molecules, wherein each reporter molecule comprises a reporter signal and a decoding tag,

wherein the reporter signals have a common property, wherein the common property allows the reporter signals to be distinguished or separated from molecules lacking the common property,

wherein the reporter signals can be altered, wherein the altered forms of each reporter signal can be distinguished from every other altered form of reporter signal,

wherein each different reporter molecule comprises a different decoding tag and a different reporter signal,

(b) a set of coding molecules, wherein each coding molecule comprises a specific binding molecule and a coding tag, wherein each specific binding molecule can interact specifically with a different analyte, wherein each coding tag can interact specifically with a different decoding tag.

81. A method comprising

(a) separating one or more reporter signals, where each reporter signal has a common property, from molecules lacking the common property in each of a plurality of samples,

(b) altering the reporter signals,

(c) detecting and distinguishing the altered forms the reporter signals from each other.

82. A set of labeled proteins wherein each labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide,

wherein the reporter signals have a common property, wherein the common property allows the labeled proteins comprising the same protein or peptide to be distinguished or separated from molecules lacking the common property,

wherein the reporter signals can be altered, wherein the altered forms of each reporter signal can be distinguished from every other altered form of reporter signal,

wherein alteration of the reporter signals alters the labeled proteins, wherein altered forms of each labeled protein can be distinguished from every other altered form of labeled protein.

83. A kit comprising a set of reporter molecules, wherein each reporter molecule comprises a reporter signal and a coupling tag,

wherein the reporter signals have a common property, wherein the common property allows the reporter signals to be distinguished or separated from molecules lacking the common property,

wherein the reporter signals can be altered, wherein the altered forms of each reporter signal can be distinguished from every other altered form of reporter signal,

wherein each different reporter molecule comprises a different coupling tag and a different reporter signal.

84. A set of labeled proteins wherein each labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide,

wherein the labeled proteins have a common property, wherein the common property allows the labeled proteins comprising the same protein or peptide to be distinguished or separated from molecules lacking the common property,

wherein the reporter signals can be altered, wherein the altered forms of each reporter signal can be distinguished from every other altered form of reporter signal,



wherein alteration of the reporter signals alters the labeled proteins, wherein altered forms of each labeled protein can be distinguished from every other altered form of labeled protein.

85. A set of labeled proteins wherein each labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide,

wherein the reporter signals can be altered, wherein the altered forms of each reporter signal can be distinguished from every other altered form of reporter signal,

wherein alteration of the reporter signals alters the labeled proteins, wherein altered forms of each labeled protein can be distinguished from every other altered form of labeled protein.

86. A set of labeled proteins wherein each labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide,

wherein the reporter signals have a common property, wherein the common property allows the labeled proteins comprising the same protein or peptide to be distinguished or separated from molecules lacking the common property.

87. A labeled protein wherein the labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide,

wherein the labeled protein has a common property, wherein the common property allows the labeled protein to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal can be altered,

wherein alteration of the reporter signals alters the labeled protein, wherein altered form of the labeled protein can be distinguished from the unaltered form of labeled protein.

88. A method comprising

(a) separating a set of labeled proteins, wherein each labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide,

wherein each reporter signal has a common property, wherein the common property allows the labeled proteins comprising the same protein or peptide to be distinguished or separated from molecules lacking the common property,

(b) altering the reporter signals, thereby altering the labeled proteins,

(c) detecting and distinguishing the altered forms of the labeled proteins from each other.

89. The method of claim 88 further comprising, prior to step (a), attaching the reporter signals to one or more proteins, one or more peptides, or one or more proteins and peptides.

90. The method of claim 89 wherein steps are repeated one or more times using a different set of reporter signals each time.

91. The method of claim 90 wherein, prior to step (a), the different sets of reporter signals are attached to proteins or peptides in different samples.

92. The method of claim 91 wherein the different sets of reporter signals each comprise the same reporter signals.

93. The method of claim 90 wherein the sets of reporter signals each contain a single reporter signal.

94. A set of labeled proteins wherein each labeled protein comprises a protein or a peptide and a reporter signal attached to the protein or peptide,

wherein the reporter signals comprise peptides, wherein the reporter signal peptides have the same mass-to-charge ratio.

95. A method comprising

(a) separating one or more labeled proteins, wherein each labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide, wherein each reporter signal has a common property, wherein the common property allows the labeled proteins comprising the same protein or peptide to be distinguished or separated from molecules lacking the common property in each of one or more samples,

(b) altering the reporter signals, thereby altering the labeled proteins,

(c) detecting and distinguishing the altered forms the labeled proteins from each other.

96. The method of claim 95 wherein the pattern of the presence, amount, presence and amount, or absence of labeled proteins in one of the samples constitutes a catalog of proteins in the sample.

97. The method of claim 96 wherein the pattern of the presence, amount, presence and amount, or absence of labeled proteins in a second one of the samples

constitutes a catalog of proteins in the second sample, wherein the catalog of proteins in the first sample is a first catalog and the catalog of proteins in the second sample is a second catalog,

the method further comprising comparing the first catalog and the second catalog.

98. A method comprising

(a) separating a set of labeled proteins, wherein each labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide,

wherein each labeled protein has a common property, wherein the common property allows the labeled proteins comprising the same protein or peptide to be distinguished or separated from molecules lacking the common property,

(b) altering the reporter signals, thereby altering the labeled proteins,

(c) detecting and distinguishing the altered forms of the labeled proteins from each other.

99. A method comprising

(a) altering labeled proteins, wherein each labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide, wherein the labeled proteins are altered by altering the reporter signals,

(b) detecting and distinguishing the altered forms of the labeled proteins from each other.

100. A method of detecting a protein or peptide, the method comprising

(a) altering a labeled protein, wherein the labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide, wherein the labeled protein is altered by altering the reporter signal,

(b) detecting and distinguishing the altered form of the labeled protein from the unaltered form of labeled protein.

101. The method of claim 100 further comprising,

detecting the unaltered form of labeled protein.

102. A method of detecting a protein, the method comprising,

detecting a labeled protein, wherein the labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide, wherein the labeled protein is altered by altering the reporter signal,

detecting an altered form of the labeled protein, wherein the labeled protein is altered by altering the reporter signal, and

identifying the protein based on the characteristics of the labeled protein and altered form of the labeled protein.

103. The method of claim 102 wherein the labeled protein and altered form of the labeled protein are detected by detecting the mass-to-charge ratio of the labeled protein and the mass-to-charge ratio of the altered form of the labeled protein or the mass-to-charge ratio of the altered form of the reporter signal.

104. A method comprising

(a) separating one or more labeled proteins from other molecules, wherein the labeled proteins are derived from one or more samples, wherein each labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide,

(b) altering the reporter signals, thereby altering the labeled proteins,

(c) detecting and distinguishing the altered forms the labeled proteins from each other.

105. The method of claim 104 further comprising, prior to step (a),

associating one or more reporter signals with one or more proteins, one or more peptides, or one or more proteins and peptides from each of the one or more samples.

106. The method of claim 104 wherein the one or more labeled proteins are derived from a single sample.

107. The method of claim 106 wherein a single labeled protein is distinguished or separated from other molecules.

108. The method of claim 106 wherein a plurality of labeled proteins are distinguished or separated from other molecules.

109. The method of claim 106 wherein the detected altered forms of the labeled proteins constitute a catalog of proteins in the sample.

110. The method of claim 104 wherein one or more labeled proteins are derived from each of a plurality of samples.

111. The method of claim 110 wherein a single labeled protein derived from each of the samples is distinguished or separated from other molecules.

112. The method of claim 110 wherein a plurality of labeled proteins derived from each of the samples are distinguished or separated from other molecules.

113. The method of claim 110 wherein the detected altered forms of the labeled proteins derived from each sample constitute a catalog of proteins in the sample.

114. A catalog of proteins and peptides comprising,  
proteins and peptides in a sample detected by

(a) separating one or more labeled proteins from other molecules, wherein the labeled proteins are derived from the sample, wherein each labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide,

(b) altering the reporter signals, thereby altering the labeled proteins,

(c) detecting and distinguishing the altered forms the labeled proteins from each other.

115. A catalog of proteins and peptides comprising,  
proteins and peptides in one or more samples detected by

(a) separating one or more labeled proteins from other molecules, wherein the labeled proteins are derived from the one or more samples, wherein each labeled protein comprises a protein or peptide and a reporter signal attached to the protein or peptide,

(b) altering the reporter signals, thereby altering the labeled proteins,

(c) detecting and distinguishing the altered forms the labeled proteins from each other.

116. A method of producing a protein signature, the method comprising

(a) treating a protein sample to produce protein fragments,

wherein the protein fragments comprise a set of target protein fragments,  
wherein the target protein fragments can be altered, wherein the altered forms of the target protein fragments can be distinguished from the other altered forms of the target protein fragments,

(b) mixing the target protein fragments with a set of reporter signal calibrators,

wherein each target protein fragment shares a common property with at least one of the reporter signal calibrators, wherein the common property allows the target protein fragments and reporter signal calibrators having the common property to be distinguished or separated from molecules lacking the common property, wherein the target protein fragment and reporter signal calibrator that share a common property correspond to each other,

wherein the reporter signal calibrators can be altered, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property,

(c) separating the target protein fragments and reporter signal calibrators from other molecules based on the common properties of the target protein fragments and reporter signal calibrators,

(d) altering the target protein fragments and reporter signal calibrators,

(e) detecting the altered forms of the target protein fragments and reporter signal calibrators,

wherein the presence, absence, amount, or presence and amount of the altered forms of the target protein fragments indicates the presence, absence, amount, or presence and amount in the protein sample of the target protein fragments from which the altered forms of the target protein fragments are derived, wherein the presence, absence, amount, or presence and amount of the target protein fragments in the protein sample constitutes a protein signature of the protein sample.

117. The method of claim 116 wherein a predetermined amount of each reporter signal calibrator is mixed with the target protein fragments, wherein the amount of each altered form of reporter signal calibrator detected provides a standard for assessing the amount of the altered form of the corresponding target protein fragment.

118. The method of claim 117 wherein the amount of at least two of the reporter signal calibrators is different.

119. The method of claim 117 wherein the relative amount each reporter signal calibrator is based on the relative amount of each corresponding target protein fragment expected to be in the protein sample.

120. The method of claim 117 wherein the amount of each of the reporter signal calibrators is the same.

121. The method of claim 116 wherein the protein fragments are produced by protease digestion of the protein sample.

122. The method of claim 121 wherein the protein fragments are produced by digestion of the protein sample with a serine protease.

123. The method of claim 122 wherein the serine protease is trypsin.

124. The method of claim 121 wherein the protein fragments are produced by digestion of the protein sample with Factor Xa or Enterokinase.

125. The method of claim 116 wherein the protein fragments are produced by cleavage at a photocleavable amino acid.

126. The method of claim 116 wherein the set of target protein fragments comprises two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, nine or more, ten or more, twenty or more, thirty or more, forty or more, fifty or more, sixty or more, seventy or more, eighty or more, ninety or more, or one hundred or more different target protein fragments.

127. The method of claim 116 further comprising comparing the protein signature to one or more other protein signatures.

128. The method of claim 116 wherein at least one of the target protein fragments comprises at least one modified amino acid.

129. The method of claim 128 wherein the modified amino acid is a phosphorylated amino acid, an acylated amino acid, or a glycosylated amino acid.

130. The method of claim 128 wherein at least one of the target protein fragments is the same as the target protein fragment comprising the modified amino acid except for the modified amino acid.

131. The method of claim 116 further comprising performing steps (a) through (e) on a control protein sample, identifying differences between the protein signatures produced from the protein sample and the control protein sample.

132. The method of claim 116 further comprising performing steps (a) through (e) on a plurality of protein samples.

133. The method of claim 132 further comprising identifying differences between the protein signatures produced from the protein samples.

134. The method of claim 132 further comprising performing steps (a) through (e) on a control protein sample, identifying differences between the protein signatures produced from the protein samples and the control protein sample.

135. The method of claim 134 wherein the differences are differences in the presence, amount, presence and amount, or absence of target protein fragments in the protein samples and the control protein sample.

136. The method of claim 132 wherein the steps (a) through (e) are performed on a control protein sample and a tester protein sample,

wherein the tester protein sample, or the source of the tester protein sample, is treated, prior to step (a), so as to destroy, disrupt or eliminate one or more protein molecules in the tester protein sample,

wherein the target protein fragments corresponding to the destroyed, disrupted, or eliminated protein molecules will be produced from the control protein sample but not the tester protein sample.

137. The method of claim 136 wherein the tester protein sample is treated so as to destroy, disrupt or eliminate one or more protein molecules in the tester protein sample.

138. The method of claim 137 wherein one or more protein molecules in the tester sample are eliminated by separating the one or more protein molecules from the tester protein sample.

139. The method of claim 138 wherein the one or more protein molecules are separated by affinity separation.

140. The method of claim 136 wherein the source of the tester protein sample is treated so as to destroy, disrupt or eliminate one or more protein molecules in the tester protein sample.

141. The method of claim 140 wherein the treatment of the source is accomplished by exposing cells from which the tester sample will be derived with a compound, composition, or condition that will reduce or eliminate expression of one or more genes.

142. The method of claim 136 further comprising identifying differences in the target protein fragments in the control protein sample and tester protein sample.

143. The method of claim 132 further comprising identifying differences between the target protein fragments in the protein samples.



144. The method of claim 132 wherein the plurality of protein samples are produced by a separation procedure, wherein the separation procedure comprises liquid chromatography, gel electrophoresis, two-dimensional chromatography, two-dimensional gel electrophoresis, isoelectric focusing, thin layer chromatography, centrifugation, filtration, ion chromatography, immunoaffinity chromatography, membrane separation, or a combination of these.

145. The method of claim 144 wherein the protein samples are different fractions or samples produced by the same separation procedure.

146. The method of claim 116 further comprising performing steps (a) through (e) on a second protein sample.

147. The method of claim 116 further comprising producing a second protein signature from a second protein sample and comparing the first protein signature and second protein signature, wherein differences in the first and second protein signatures indicate differences in source or condition of the source of the first and second protein samples.

148. The method of claim 116 further comprising producing a second protein signature from a second protein sample and comparing the first protein signature and second protein signature, wherein differences in the first and second protein signatures indicate differences in protein modification of the first and second protein samples.

149. The method of claim 148 wherein the second protein sample is a sample from the same type of cells as the first protein sample except that the cells from which the first protein sample is derived are modification-deficient relative to the cells from which the second protein sample is derived.

150. The method of claim 148 wherein the second protein sample is a sample from a different type of cells than the first protein sample, and wherein the cells from which the first protein sample is derived are modification-deficient relative to the cells from which the second protein sample is derived.

151. The method of claim 116 wherein the protein sample is derived from one or more cells.

152. The method of claim 151 wherein the protein signature indicates the physiological state of the cells.

153. The method of claim 151 wherein the protein signature indicates the effect of a treatment of the cells.

154. The method of claim 153 wherein the cells are derived from an organism, wherein the cells are treated by treating the organism.

155. The method of claim 154 wherein the organism is treated by administering a compound to the organism.

156. The method of claim 154 wherein the organism is human.

157. The method of claim 116 wherein the protein sample is produced by a separation procedure, wherein the separation procedure comprises liquid chromatography, gel electrophoresis, two-dimensional chromatography, two-dimensional gel electrophoresis, isoelectric focusing, thin layer chromatography, centrifugation, filtration, ion chromatography, immunoaffinity chromatography, membrane separation, or a combination of these.

158. The method of claim 116 wherein the set of reporter signal calibrators consists of a single reporter signal calibrator.

159. The method of claim 158 wherein the protein signature of the protein sample represents the presence, absence, amount, or presence and amount of the target protein fragment in the protein sample that corresponds to the reporter signal calibrator.

160. A method of producing a protein signature, the method comprising detecting altered forms of target protein fragments and reporter signal calibrators,

wherein the altered forms of the target protein fragments can be distinguished from the other altered forms of the target protein fragments, wherein each target protein fragment shares a common property with at least one of the reporter signal calibrators, wherein the common property allows the target protein fragments and reporter signal calibrators having the common property to be distinguished or separated from molecules lacking the common property, wherein the target protein fragment and reporter signal calibrator that share a common property correspond to each other, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property,

wherein the presence, absence, amount, or presence and amount of the altered forms of the target protein fragments indicates the presence, absence, amount, or presence and amount in a protein sample of the target protein fragments from which the altered forms of the target protein fragments are derived, wherein the presence, absence, amount, or presence and amount of the target protein fragments in the protein sample constitutes a protein signature of the protein sample.

161. The method of claim 160 wherein the target protein fragments and reporter signal calibrators are distinguished or separated from other molecules based on the common properties of the target protein fragments and reporter signal calibrators.

162. The method of claim 161 wherein the target protein fragments and reporter signal calibrators are altered following separation.

163. The method of claim 160 wherein the target protein fragments are produced by treating the protein sample.

164. A method of producing a protein signature, the method comprising

(a) treating a protein sample to produce protein fragments,

wherein the protein fragments comprise a set of target protein fragments, wherein the target protein fragments can be altered, wherein the altered forms of the target protein fragments can be distinguished from the other altered forms of the target protein fragments,

(b) separating the target protein fragments from other protein fragments in the protein sample,

(c) altering the target protein fragments,

(d) detecting the altered forms of the target protein fragments,

wherein the presence, absence, amount, or presence and amount of the altered forms of the target protein fragments indicates the presence, absence, amount, or presence and amount in the protein sample of the target protein fragments from which the altered forms of the target protein fragments are derived, wherein the presence, absence, amount, or presence and amount of the target protein fragments in the protein sample constitutes a protein signature of the protein sample.

165. The method of claim 164 further comprising, prior to or simultaneous with step (b), mixing the target protein fragments with a set of reporter signal calibrators,

wherein each target protein fragment shares a common property with at least one of the reporter signal calibrators, wherein the common property allows the target protein fragments and reporter signal calibrators having the common property to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal calibrators can be altered, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property.

166. A method of producing a protein signature, the method comprising  
(a) separating a plurality of target protein fragments from other protein fragments in a protein sample,

(b) altering the target protein fragments,

(c) detecting the altered forms of the target protein fragments,

wherein the presence, absence, amount, or presence and amount of the altered forms of the target protein fragments indicates the presence, absence, amount, or presence and amount in the protein sample of the target protein fragments from which the altered forms of the target protein fragments are derived, wherein the presence, absence, amount, or presence and amount of the target protein fragments in the protein sample constitutes a protein signature of the protein sample.

167. A method of analyzing a protein sample, the method comprising  
(a) mixing a protein sample with a predetermined amount of a reporter signal calibrator,

wherein the protein sample has a known amount of protein, wherein the protein sample comprises a target protein fragment,

wherein the target protein fragment can be altered, wherein the reporter signal calibrator can be altered, wherein the altered form of the reporter signal calibrator can be distinguished from the altered form of the target protein fragment,

(b) altering the target protein fragment and reporter signal calibrator,

(c) detecting the altered forms of the target protein fragment and reporter signal calibrator.

168. The method of claim 167 further comprising determining the ratio of the amount of the target protein fragment and the amount of the reporter signal calibrator detected, and

comparing the determined ratio with the predicted ratio of the amount of the target protein fragment and the amount of the reporter signal calibrator,

wherein the predicted ratio is based on the predicted amount of target protein fragment in the protein sample and the predetermined amount of reporter signal calibrator, wherein the predicted amount of target protein fragment is the amount of target protein fragment the protein sample would have if the known amount of protein in the protein sample consisted of the target protein fragment,

wherein the difference between the determined ratio and the predicted ratio is a measure of the purity of the protein sample for the target protein fragment, wherein the closer the determined ratio is to the predicted ratio, the purer the protein sample.

169. A method of analyzing a protein sample, the method comprising

(a) treating a protein sample to produce protein fragments, wherein the protein sample has a known amount of protein, wherein the protein sample comprises a target protein, wherein the protein fragments comprise a target protein fragment derived from the target protein,

(b) mixing the protein sample with a predetermined amount of a reporter signal calibrator,

wherein the target protein fragment can be altered, wherein the reporter signal calibrator can be altered, wherein the altered form of the reporter signal calibrator can be distinguished from the altered form of the target protein fragment,

(b) altering the target protein fragment and reporter signal calibrator,

(c) detecting the altered forms of the target protein fragment and reporter signal calibrator.

170. The method of claim 169 further comprising determining the ratio of the amount of the target protein fragment and the amount of the reporter signal calibrator detected, and

comparing the determined ratio with the predicted ratio of the amount of the target protein fragment and the amount of the reporter signal calibrator,

wherein the predicted ratio is based on the predicted amount of target protein fragment in the protein sample and the predetermined amount of reporter signal calibrator, wherein the predicted amount of target protein fragment is the amount of target protein fragment the protein sample would have if the known amount of protein in the protein sample consisted of the target protein,

wherein the difference between the determined ratio and the predicted ratio is a measure of the purity of the protein sample for the target protein, wherein the closer the determined ratio is to the predicted ratio, the purer the protein sample.

171. A set of reporter signal calibrators,

wherein each reporter signal calibrator shares a common property with a target protein fragment in a set of target protein fragments, wherein the common property allows the target protein fragments and reporter signal calibrators having the common property to be distinguished or separated from molecules lacking the common property, wherein the target protein fragment and reporter signal calibrator that share a common property correspond to each other,

wherein the target protein fragments can be altered, wherein the altered forms of the target protein fragments can be distinguished from the other altered forms of the target protein fragments,

wherein the reporter signal calibrators can be altered, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property.

172. The set of claim 171 wherein the set includes a predetermined amount of each reporter signal calibrator.

173. The set of claim 172 wherein the amount of at least two of the reporter signal calibrators is different.

174. The set of claim 172 wherein the relative amount each reporter signal calibrator is based on the relative amount of each corresponding target protein fragment expected to be in the protein sample.

175. The set of claim 172 wherein the amount of each of the reporter signal calibrators is the same.

176. A kit for producing a protein signature, the kit comprising

(a) a set of reporter signal calibrators,

wherein each reporter signal calibrator shares a common property with a target protein fragment in a set of target protein fragments, wherein the common property allows the target protein fragments and reporter signal calibrators having the common property to be distinguished or separated from molecules lacking the common property, wherein the target protein fragment and reporter signal calibrator that share a common property correspond to each other,

wherein the target protein fragments can be altered, wherein the altered forms of the target protein fragments can be distinguished from the other altered forms of the target protein fragments,

wherein the reporter signal calibrators can be altered, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property,

(b) one or more reagents for treating a protein sample to produce protein fragments.

177. A mixture comprising

a set of reporter signal calibrators and a set of target protein fragments,

wherein each reporter signal calibrator shares a common property with a target protein fragment in the set of target protein fragments, wherein the common property allows the target protein fragments and reporter signal calibrators having the common property to be distinguished or separated from molecules lacking the common property, wherein the target protein fragment and reporter signal calibrator that share a common property correspond to each other,

wherein the target protein fragments can be altered, wherein the altered forms of the target protein fragments can be distinguished from the other altered forms of the target protein fragments,

wherein the reporter signal calibrators can be altered, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property.

178. A set of target protein fragments,

wherein each target protein fragment shares a common property with a reporter signal calibrator in a set of reporter signal calibrators, wherein the common property allows the target protein fragments and reporter signal calibrators having the common property to be distinguished or separated from molecules lacking the common property, wherein the target protein fragment and reporter signal calibrator that share a common property correspond to each other,

wherein the target protein fragments can be altered, wherein the altered forms of the target protein fragments can be distinguished from the other altered forms of the target protein fragments,

wherein the reporter signal calibrators can be altered, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property.

179. A method of producing a protein signature, the method comprising

(a) treating a protein sample to produce protein fragments,

wherein the protein fragments comprise a set of target protein fragments, wherein each of the target protein fragments can be altered, wherein the altered forms of each target protein fragment can be distinguished from every other altered form of target protein fragment,

(b) mixing the target protein fragments with a set of reporter signal calibrators,

wherein each target protein fragment shares a common property with at least one of the reporter signal calibrators, wherein the common property allows each of the target protein fragments and reporter signal calibrators having the common property to be distinguished or separated from molecules lacking the common property, wherein the target protein fragment and reporter signal calibrator that share a common property correspond to each other,

wherein each of the reporter signal calibrators can be altered, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property,



(c) separating the target protein fragments and reporter signal calibrators from other molecules based on the common properties of the target protein fragments and reporter signal calibrators,

(d) altering the target protein fragments and reporter signal calibrators,

(e) detecting the altered forms of the target protein fragments and reporter signal calibrators,

wherein the presence, absence, amount, or presence and amount of the altered forms of the target protein fragments indicates the presence, absence, amount, or presence and amount in the protein sample of the target protein fragments from which the altered forms of the target protein fragments are derived, wherein the presence, absence, amount, or presence and amount of the target protein fragments in the protein sample constitutes a protein signature of the protein sample.

180. A method of producing a protein signature, the method comprising detecting altered forms of target protein fragments and reporter signal calibrators,

wherein the altered forms of each target protein fragment can be distinguished from every other altered form of target protein fragment, wherein each target protein fragment shares a common property with at least one of the reporter signal calibrators, wherein the common property allows each of the target protein fragments and reporter signal calibrators having the common property to be distinguished or separated from molecules lacking the common property, wherein the target protein fragment and reporter signal calibrator that share a common property correspond to each other, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property,

wherein the presence, absence, amount, or presence and amount of the altered forms of the target protein fragments indicates the presence, absence, amount, or presence and amount in a protein sample of the target protein fragments from which the altered forms of the target protein fragments are derived, wherein the presence, absence, amount, or presence and amount of the target protein fragments in the protein sample constitutes a protein signature of the protein sample.

181. A method of producing a protein signature, the method comprising

(a) treating a protein sample to produce protein fragments,  
wherein the protein fragments comprise a set of target protein fragments,  
wherein each of the target protein fragments can be altered, wherein the altered forms  
of each target protein fragment can be distinguished from every other altered form of  
target protein fragment,

(b) separating the target protein fragments from other protein fragments in the  
protein sample,

(c) altering the target protein fragments,

(d) detecting the altered forms of the target protein fragments,

wherein the presence, absence, amount, or presence and amount of the altered  
forms of the target protein fragments indicates the presence, absence, amount, or  
presence and amount in the protein sample of the target protein fragments from which  
the altered forms of the target protein fragments are derived, wherein the presence,  
absence, amount, or presence and amount of the target protein fragments in the protein  
sample constitutes a protein signature of the protein sample.

182. The method of claim 181 further comprising, prior to or simultaneous with  
step (b), mixing the target protein fragments with a set of reporter signal calibrators,

wherein each target protein fragment shares a common property with at least  
one of the reporter signal calibrators, wherein the common property allows each of the  
target protein fragments and reporter signal calibrators having the common property to  
be distinguished or separated from molecules lacking the common property,

wherein each of the reporter signal calibrators can be altered, wherein the  
altered form of each reporter signal calibrator can be distinguished from the altered  
form of the target protein fragment with which the reporter signal calibrator shares a  
common property.

183. A set of reporter signal calibrators,

wherein each reporter signal calibrator shares a common property with a target  
protein fragment in a set of target protein fragments, wherein the common property  
allows each of the target protein fragments and reporter signal calibrators having the  
common property to be distinguished or separated from molecules lacking the common  
property, wherein the target protein fragment and reporter signal calibrator that share a  
common property correspond to each other,

wherein each of the target protein fragments can be altered, wherein the altered forms of each target protein fragment can be distinguished from every other altered form of target protein fragment,

wherein each of the reporter signal calibrators can be altered, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property.

184. A kit for producing a protein signature, the kit comprising

(a) a set of reporter signal calibrators,

wherein each reporter signal calibrator shares a common property with a target protein fragment in a set of target protein fragments, wherein the common property allows each of the target protein fragments and reporter signal calibrators having the common property to be distinguished or separated from molecules lacking the common property, wherein the target protein fragment and reporter signal calibrator that share a common property correspond to each other,

wherein each of the target protein fragments can be altered, wherein the altered forms of each target protein fragment can be distinguished from every other altered form of target protein fragment,

wherein each of the reporter signal calibrators can be altered, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property,

(b) one or more reagents for treating a protein sample to produce protein fragments.

185. A mixture comprising

a set of reporter signal calibrators and a set of target protein fragments,

wherein each reporter signal calibrator shares a common property with a target protein fragment in the set of target protein fragments, wherein the common property allows each of the target protein fragments and reporter signal calibrators having the common property to be distinguished or separated from molecules lacking the common property, wherein the target protein fragment and reporter signal calibrator that share a common property correspond to each other,

wherein each of the target protein fragments can be altered, wherein the altered forms of each target protein fragment can be distinguished from every other altered form of target protein fragment,

wherein each of the reporter signal calibrators can be altered, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property.

186. A set of target protein fragments,

wherein each target protein fragment shares a common property with a reporter signal calibrator in a set of reporter signal calibrators, wherein the common property allows each of the target protein fragments and reporter signal calibrators having the common property to be distinguished or separated from molecules lacking the common property, wherein the target protein fragment and reporter signal calibrator that share a common property correspond to each other,

wherein each of the target protein fragments can be altered, wherein the altered forms of each target protein fragment can be distinguished from every other altered form of target protein fragment,

wherein each of the reporter signal calibrators can be altered, wherein the altered form of each reporter signal calibrator can be distinguished from the altered form of the target protein fragment with which the reporter signal calibrator shares a common property.

187. A set of nucleic acid molecules wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides.

188. The set of claim 187 wherein each nucleic acid molecule further comprises expression sequences, wherein the expression sequences are operably linked to the nucleotide segment such that the amino acid segment can be expressed.

189. The set of claim 188 wherein the expression sequences comprise translation expression sequences.

190. The set of claim 189 wherein the expression sequences further comprise transcription expression sequences.

191. The set of claim 188 wherein the amino acid segment can be expressed in vitro.

192. The set of claim 188 wherein the amino acid segment can be expressed in vivo.

193. The set of claim 192 wherein the amino acid segment can be expressed in cell culture.

194. The set of claim 188 wherein the expression sequences of each nucleic acid molecule are different.

195. The set of claim 194 wherein the different expression sequences are differently regulated.

196. The set of claim 194 wherein the expression sequences are similarly regulated.

197. The set of claim 196 wherein a plurality of the expression sequences are expression sequences of, or derived from, genes expressed as part of the same expression cascade.

198. The set of claim 188 wherein the expression sequences of each nucleic acid molecule are the same.

199. The set of claim 198 wherein the expression sequences are similarly regulated.

200. The set of claim 188 wherein the expression sequences of at least two nucleic acid molecules are different.

201. The set of claim 188 wherein the expression sequences of at least two nucleic acid molecules are the same.

202. The set of claim 187 wherein each nucleic acid molecule further comprises replication sequences, wherein the replication sequences allow replication of the nucleic acid molecules.

203. The set of claim 202 wherein the nucleic acid molecules can be replicated in vitro.

204. The set of claim 202 wherein the nucleic acid molecules can be replicated in vivo.

205. The set of claim 204 wherein the nucleic acid molecules can be replicated in cell culture.

206. The set of claim 187 wherein each nucleic acid molecule further comprises integration sequences, wherein the integration sequences allow integration of the nucleic acid molecules into other nucleic acids.

207. The set of claim 206 wherein the nucleic acid molecules can be integrated into a chromosome.

208. The set of claim 207 wherein the nucleic acid molecules can be integrated into a chromosome at a predetermined location.

209. The set of claim 187 wherein the nucleic acids molecules are produced by replicating nucleic acids in one or more nucleic acid samples.

210. The set of claim 209 wherein the nucleic acids are replicated using pairs of primers, wherein each of the first primers in the primer pairs used to produce the nucleic acid molecules comprises a nucleotide sequence encoding the reporter signal peptide.

211. The set of claim 210 wherein each first primer further comprises expression sequences.

212. The set of claim 211 wherein the nucleotide sequence of each first primer also encodes an epitope tag.

213. The set of claim 187 wherein each amino acid segment further comprises an epitope tag.

214. The set of claim 213 wherein the epitope tag of each amino acid segment is different.

215. The set of claim 213 wherein the epitope tag of each amino acid segment is the same.

216. The set of claim 213 wherein the epitope tag of at least two amino acid segments are different.

217. The set of claim 213 wherein the epitope tag of at least two amino acid segments are the same.

218. The set of claim 187 wherein the reporter signal peptide of each amino acid segment is different.

219. The set of claim 187 wherein the reporter signal peptide of each amino acid segment is the same.

220. The set of claim 187 wherein the reporter signal peptide of at least two amino acid segments are different.

221. The set of claim 187 wherein the reporter signal peptide of at least two amino acid segments are the same.

222. The set of claim 187 wherein the nucleic acid molecules are in cells.

223. The set of claim 222 wherein each nucleic acid molecule is in a different cell.

224. The set of claim 222 wherein each nucleic acid molecule is in the same cell.

225. The set of claim 224 wherein each nucleic acid molecule further comprises expression sequences, wherein the expression sequences are operably linked to the nucleotide segment such that the amino acid segment can be expressed.

226. The set of claim 225 wherein the expression sequences of each nucleic acid molecule are different.

227. The set of claim 226 wherein the expression sequences are similarly regulated.

228. The set of claim 227 wherein a plurality of the expression sequences are expression sequences of, or derived from, genes expressed as part of the same expression cascade.

229. The set of claim 222 wherein the nucleic acid molecules are integrated into a chromosome of the cell.

230. The set of claim 229 wherein the nucleic acid molecules are integrated into the chromosome at a predetermined location.

231. The set of claim 229 wherein the chromosome is an artificial chromosome.
232. The set of claim 222 wherein the nucleic acid molecules are, or are integrated into, a plasmid.
233. The set of claim 222 wherein the cells are in cell lines.
234. The set of claim 233 wherein each nucleic acid molecule is in a different cell line.
235. The set of claim 233 wherein each nucleic acid molecule is in the same cell line.
236. The set of claim 187 wherein the nucleic acid molecules are in organisms.
237. The set of claim 236 wherein each nucleic acid molecule is in a different organism.
238. The set of claim 236 wherein each nucleic acid molecule is in the same organism.
239. The set of claim 238 wherein each nucleic acid molecule further comprises expression sequences, wherein the expression sequences are operably linked to the nucleotide segment such that the amino acid segment can be expressed.
240. The set of claim 239 wherein the expression sequences of each nucleic acid molecule are different.
241. The set of claim 240 wherein the expression sequences are similarly regulated.
242. The set of claim 241 wherein a plurality of the expression sequences are expression sequences of, or derived from, genes expressed as part of the same expression cascade.
243. The set of claim 236 wherein the nucleic acid molecules are integrated into a chromosome of the organism.
244. The set of claim 243 wherein the nucleic acid molecules are integrated into the chromosome at a predetermined location.
245. The set of claim 243 wherein the chromosome is an artificial chromosome.
246. The set of claim 236 wherein the nucleic acid molecules are, or are integrated into, a plasmid.



247. The set of claim 236 wherein each nucleic acid molecule is in a different organism.

248. The set of claim 236 wherein each nucleic acid molecule is in the same organism.

249. The set of claim 187 wherein the nucleic acid molecules are in cells of an organism.

250. The set of claim 249 wherein the nucleic acid molecules are in substantially all of the cells of the organism.

251. The set of claim 249 wherein the nucleic acid molecules are in some of the cells of the organism.

252. The set of claim 249 wherein the amino acid segments are expressed in substantially all of the cells of the organism.

253. The set of claim 249 wherein the amino acid segments are expressed in some of the cells of the organism.

254. The set of claim 187 wherein the protein or peptide of interest of each amino acid segment is different.

255. The set of claim 187 wherein the protein or peptide of interest of each amino acid segment is the same.

256. The set of claim 187 wherein the protein or peptide of interest of at least two amino acid segments are different.

257. The set of claim 187 wherein the protein or peptide of interest of at least two amino acid segments are the same.

258. The set of claim 254 wherein the proteins or peptides of interest are related.

259. The set of claim 258 wherein the proteins or peptides of interest are proteins produced in the same cascade.

260. The set of claim 258 wherein the proteins or peptides of interest are proteins expressed under the same conditions.

261. The set of claim 258 wherein the proteins or peptides of interest are proteins associated with the same disease.

262. The set of claim 258 wherein the proteins or peptides of interest are proteins associated with the same cell type.

263. The set of claim 258 wherein the proteins or peptides of interest are proteins associated with the same tissue type.

264. The set of claim 258 wherein the proteins or peptides of interest are proteins in the same enzymatic pathway.

265. The set of claim 187 wherein the nucleotide segment encodes a plurality of amino acid segments each comprising a reporter signal peptide and a protein or peptide of interest.

266. The set of claim 265 wherein the protein or peptide of interest of at least two of the amino acid segments in one of the nucleotide segments are different.

267. The set of claim 265 wherein the protein or peptide of interest of the amino acid segments in one of the nucleotide segments are different.

268. The set of claim 265 wherein the protein or peptide of interest of at least two of the amino acid segments in each of the nucleotide segments are different.

269. The set of claim 265 wherein the protein or peptide of interest of the amino acid segments in each of the nucleotide segments are different.

270. The set of claim 265 wherein the set consists of a single nucleic acid molecule.

271. The set of claim 187 wherein the set consists of a single nucleic acid molecule, wherein the nucleic acid molecule comprises a plurality of nucleotide segments each encoding an amino acid segment.

272. The set of claim 187 wherein the amino acid segment comprises a cleavage site near the junction between the reporter signal peptide and the protein or peptide of interest.

273. The set of claim 272 wherein the cleavage site is a trypsin cleavage site.

274. The set of claim 272 wherein the cleavage site is at the junction between the reporter signal peptide and the protein or peptide of interest.

275. The set of claim 187 wherein each amino acid segment further comprises a self-cleaving segment.

276. The set of claim 275 wherein the self-cleaving segment is between the reporter signal peptide and the protein or peptide of interest.

277. The set of claim 275 wherein the self-cleaving segment is an intein segment.

278. A set of nucleic acid molecules wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein alteration of the reporter signal peptides alters the amino acid segments, wherein the altered form of each amino acid segment can be distinguished from the altered forms of the other amino acid segments.

279. A set of nucleic acid molecules wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the amino acid segments have a common property, wherein the common property allows the amino acid segments to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides.

280. A set of nucleic acid molecules wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the amino acid segments have a common property, wherein the common property allows the amino acid segments to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein alteration of the reporter signal peptides alters the amino acid segments, wherein the altered form of each amino acid segment can be distinguished from the altered forms of the other amino acid segments.

281. A set of nucleic acid molecules wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the amino acid segments each comprise an amino acid subsegment, wherein each amino acid subsegment comprises a portion of the protein or peptide of interest and all or a portion of the reporter signal peptide,

wherein the amino acid subsegments have a common property, wherein the common property allows the amino acid subsegments to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides.

282. A set of nucleic acid molecules wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the amino acid segments each comprise an amino acid subsegment, wherein each amino acid subsegment comprises a portion of the protein or peptide of interest and all or a portion of the reporter signal peptide,

wherein the amino acid subsegments have a common property, wherein the common property allows the amino acid subsegments to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein alteration of the reporter signal peptides alters the amino acid subsegments, wherein the altered form of each amino acid subsegment can be distinguished from the altered forms of the other amino acid subsegments.

283. A set of amino acid segments wherein each amino acid segment comprises a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides.

284. The set of claim 283 wherein the amino acid segment is a protein or peptide.

285. The set of claim 283 wherein the set consists of a single amino acid segment, wherein the amino acid segment comprises a plurality of reporter signal peptides.

286. A cell comprising a set of nucleic acid molecules wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides.

287. A set of cells wherein each cell comprises a nucleic acid molecule wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides.

288. The set of claim 287 wherein each cell further comprises additional nucleic acid molecules.

289. The set of claim 287 wherein the set consists of a single cell, wherein the cell comprises a plurality of nucleic acid molecules.

290. The set of claim 287 wherein the set consists of a single cell, wherein the cell comprises a set of nucleic acid molecules, wherein the set of nucleic acid molecules consists of a single nucleic acid molecule, wherein the nucleic acid molecule encodes a plurality of nucleic acid segments.

291. An organism comprising a set of nucleic acid molecules wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides.

292. A set of organisms each organism comprises a nucleic acid molecule wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides.

293. The set of claim 292 wherein each organism further comprises additional nucleic acid molecules.

294. The set of claim 292 wherein the set consists of a single organism, wherein the organism comprises a plurality of nucleic acid molecules.

295. The set of claim 292 wherein the set consists of a single organism, wherein the organism comprises a set of nucleic acid molecules, wherein the set of nucleic acid molecules consists of a single nucleic acid molecule, wherein the nucleic acid molecule encodes a plurality of nucleic acid segments.

296. A method of detecting expression, the method comprising detecting a target altered reporter signal peptide derived from one or more expression samples,

wherein the one or more expression samples collectively comprise a set of nucleic acid molecules, wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides, wherein the target altered reporter signal peptide is one of the altered reporter signal peptides,

wherein detection of the target altered reporter signal peptide indicates expression of the amino acid segment that comprises the reporter signal peptide from which the target altered reporter signal peptide is derived.

297. The method of claim 296 further comprising determining the amount of the target altered reporter signal peptide detected,

wherein the amount of the target altered reporter signal peptide indicates the amount present in the one or more expression samples of the amino acid segment that comprises the reporter signal peptide from which the target altered reporter signal peptide is derived.

298. The method of claim 297 wherein the amount of the amino acid segment present is proportional to the amount of the target altered reporter signal peptide detected.

299. The method of claim 296 further comprising detecting a plurality of the altered reporter signal peptides,

wherein detection of each altered reporter signal peptide indicates expression of the amino acid segment that comprises the reporter signal peptide from which that altered reporter signal peptide is derived.

300. The method of claim 299 further comprising determining the amount of the altered reporter signal peptides detected,

wherein the amount of each altered reporter signal peptide indicates the amount present in the one or more expression samples of the amino acid segment that comprises the reporter signal peptide from which that altered reporter signal peptide is derived.

301. The method of claim 300 wherein the amount of the amino acid segment present is proportional to the amount of the altered reporter signal peptide detected.

302. The method of claim 299 wherein the presence, absence, amount, or presence and amount of the altered forms of the reporter signal peptides indicates the presence, absence, amount, or presence and amount in the expression sample of the reporter signal peptides from which the altered forms of the reporter signal peptides are derived, wherein the presence, absence, amount, or presence and amount of the reporter signal peptides in the expression sample constitutes a protein signature of the expression sample.

303. The method of claim 302 wherein the altered forms of the reporter signal peptides are detecting using mass spectrometry.

304. The method of claim 303 wherein the altered forms of the reporter signal peptides are detected with a tandem mass spectrometer.

305. The method of claim 304 wherein the mass spectrometer includes a quadrupole set for single-ion filtering, a collision cell, and a time-of-flight spectrometer.

306. The method of claim 302 wherein the reporter signal peptides are altered by fragmentation.

307. The method of claim 306 wherein the reporter signal peptides are altered by cleavage at a photocleavable amino acid.

308. The method of claim 306 wherein the reporter signal peptides are fragmented in a collision cell.

309. The method of claim 306 wherein the reporter signal peptides are fragmented at an asparagine-proline bond, a methionine, or a phosphorylated amino acid.

310. The method of claim 302 wherein the common property is mass-to-charge ratio, wherein the reporter signal peptides are altered by altering their mass, their charge, or their mass and charge, wherein the altered forms of the reporter signal peptides can be distinguished via differences in the mass-to-charge ratio of the altered forms of the reporter signal peptides.

311. The method of claim 302 wherein there are two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, nine or more, ten or more, twenty or more, thirty or more, forty or more, fifty or more, sixty or more,



seventy or more, eighty or more, ninety or more, or one hundred or more different reporter signal peptides.

312. The method of claim 311 wherein there are ten or more different reporter signal peptides.

313. The method of claim 312 wherein each reporter signal peptide has a labile or scissile bond in a different location.

314. The method of claim 302 further comprising comparing the protein signature to one or more other protein signatures.

315. The method of claim 302 wherein the detected altered reporter signal peptides are derived from a plurality of expression samples.

316. The method of claim 315 wherein some of the detected altered reporter signal peptides derived from a control expression sample,

identifying differences between the protein signatures produced from the expression samples and the control expression sample.

317. The method of claim 316 wherein the differences are differences in the presence, amount, presence and amount, or absence of reporter signal peptides in the expression samples and the control expression sample.

318. The method of claim 315 wherein the plurality of expression samples comprises a control expression sample and a tester expression sample,

wherein the tester expression sample, or the source of the tester expression sample, is treated so as to destroy, disrupt or eliminate one or more of the amino acid segments in the tester expression sample,

wherein the reporter signal peptides corresponding to the destroyed, disrupted, or eliminated amino acid segments will be produced from the control expression sample but not the tester expression sample.

319. The method of claim 318 wherein the tester expression sample is treated so as to destroy, disrupt or eliminate one or more of the amino acid segments in the tester expression sample.

320. The method of claim 319 wherein one or more of the amino acid segments in the tester sample are eliminated by separating the one or more of the amino acid segments from the tester expression sample.

321. The method of claim 320 wherein the one or more of the amino acid segments are separated by affinity separation.

322. The method of claim 318 wherein the source of the tester expression sample is treated so as to destroy, disrupt or eliminate one or more of the amino acid segments in the tester expression sample.

323. The method of claim 322 wherein the treatment of the source is accomplished by exposing cells from which the tester sample will be derived with a compound, composition, or condition that will reduce or eliminate expression of one or more of the nucleotide segments.

324. The method of claim 318 further comprising identifying differences in the reporter signal peptides in the control expression sample and tester expression sample.

325. The method of claim 315 further comprising identifying differences between the reporter signal peptides in the expression samples.

326. The method of claim 315 wherein at least two of the expression samples, or the sources of the at least two expression samples, are subjected to different conditions.

327. The method of claim 326 wherein the sources of the expression samples are cells.

328. The method of claim 326 wherein differences in the protein signatures of the at least two expression samples indicate the effect of the different conditions.

329. The method of claim 326 wherein the different conditions are exposure to different compounds.

330. The method of claim 326 wherein the different conditions are exposure to a compound and no exposure to the compound.

331. The method of claim 302 further comprising producing a second protein signature from a second expression sample and comparing the first protein signature and second protein signature, wherein differences in the first and second protein signatures indicate differences in source or condition of the source of the first and second expression samples.

332. The method of claim 302 further comprising producing a second protein signature from a second expression sample and comparing the first protein signature

and second protein signature, wherein differences in the first and second protein signatures indicate differences in protein modification of the first and second expression samples.

333. The method of claim 332 wherein the second expression sample is a sample from the same type of cells as the first expression sample except that the cells from which the first expression sample is derived are modification-deficient relative to the cells from which the second expression sample is derived.

334. The method of claim 332 wherein the second expression sample is a sample from a different type of cells than the first expression sample, and wherein the cells from which the first expression sample is derived are modification-deficient relative to the cells from which the second expression sample is derived.

335. The method of claim 302 wherein the expression sample is derived from one or more cells.

336. The method of claim 335 wherein the protein signature indicates the physiological state of the cells.

337. The method of claim 335 wherein the protein signature indicates the effect of a treatment of the cells.

338. The method of claim 337 wherein the cells are derived from an organism, wherein the cells are treated by treating the organism.

339. The method of claim 338 wherein the organism is treated by administering a compound to the organism.

340. The method of claim 338 wherein the organism is human.

341. The method of claim 299 wherein altered reporter signal peptides are detected in a first and a second expression sample.

342. The method of claim 341 wherein the second expression sample is a sample from the same type of organism as the first expression sample.

343. The method of claim 341 wherein the second expression sample is a sample from the same type of tissue as the first expression sample.

344. The method of claim 341 wherein the second expression sample is a sample from the same organism as the first expression sample.

345. The method of claim 344 wherein the second expression sample is obtained at a different time than the first expression sample.

346. The method of claim 341 wherein the second expression sample is a sample from a different organism than the first expression sample.

347. The method of claim 341 wherein the second expression sample is a sample from a different type of tissue than the first expression sample.

348. The method of claim 341 wherein the second expression sample is a sample from a different species of organism than the first expression sample.

349. The method of claim 341 wherein the second expression sample is a sample from a different strain of organism than the first expression sample.

350. The method of claim 341 wherein the second expression sample is a sample from a different cellular compartment than the first expression sample.

351. The method of claim 296 further comprising altering the reporter signal peptides.

352. The method of claim 351 wherein the reporter signal peptides are altered by fragmentation.

353. The method of claim 352 wherein the reporter signal peptides are altered by cleavage at a photocleavable amino acid.

354. The method of claim 352 wherein the reporter signal peptides are fragmented in a collision cell.

355. The method of claim 352 wherein the reporter signal peptides are fragmented at an asparagine-proline bond, a methionine, or a phosphorylated amino acid.

356. The method of claim 296 further comprising separating the reporter signal peptides from the expression samples.

357. The method of claim 356 wherein the reporter signal peptides are distinguished or separated from the expression samples based on the common property.

358. The method of claim 296 further comprising cleaving the reporter signal peptides from the proteins or peptides of interest.

359. The method of claim 358 wherein the reporter signal peptides are distinguished or separated from the proteins or peptides of interest based on the common property.

360. The method of claim 296 further comprising cleaving the amino acid segments into a reporter signal peptide portion and a protein portion.

361. The method of claim 296 further comprising mixing two or more of the expression samples together.

362. The method of claim 296 further comprising mixing two or more amino acid segments together, wherein the mixed amino acid segments were derived from two or more different expression samples.

363. The method of claim 296 wherein expression of the amino acid segment that comprises the reporter signal peptide from which the target altered reporter signal peptide is derived identifies the expression sample from which the target altered reporter signal peptide is derived.

364. The method of claim 363 wherein the expression samples are derived from one or more cells, wherein expression of the amino acid segment that comprises the reporter signal peptide from which the target altered reporter signal peptide is derived identifies the cell from which the identified expression sample is derived.

365. The method of claim 363 wherein the expression samples are derived from one or more organisms, wherein expression of the amino acid segment that comprises the reporter signal peptide from which the target altered reporter signal peptide is derived identifies the organism from which the identified expression sample is derived.

366. The method of claim 363 wherein the expression samples are derived from one or more tissues, wherein expression of the amino acid segment that comprises the reporter signal peptide from which the target altered reporter signal peptide is derived identifies the tissue from which the identified expression sample is derived.

367. The method of claim 363 wherein the expression samples are derived from one or more cell lines, wherein expression of the amino acid segment that comprises the reporter signal peptide from which the target altered reporter signal peptide is derived identifies the cell line from which the identified expression sample is derived.

368. The method of claim 296 wherein each nucleic acid molecule further comprises expression sequences, wherein the expression sequences are operably linked to the nucleotide segment such that the amino acid segment is expressed.

369. The method of claim 368 wherein the expression sequences comprise translation expression sequences.

370. The method of claim 369 wherein the expression sequences further comprise transcription expression sequences.

371. The method of claim 368 wherein the amino acid segment is expressed in vitro.

372. The method of claim 368 wherein the amino acid segment is expressed in vivo.

373. The method of claim 372 wherein the amino acid segment is expressed in cell culture.

374. The method of claim 368 wherein the expression sequences of each nucleic acid molecule are different.

375. The method of claim 374 wherein the different expression sequences are differently regulated.

376. The method of claim 374 wherein the expression sequences are similarly regulated.

377. The method of claim 376 wherein a plurality of the expression sequences are expression sequences of, or derived from, genes expressed as part of the same expression cascade.

378. The method of claim 368 wherein the expression sequences of each nucleic acid molecule are the same.

379. The method of claim 378 wherein the expression sequences are similarly regulated.

380. The method of claim 368 wherein the expression sequences of at least two nucleic acid molecules are different.

381. The method of claim 368 wherein the expression sequences of at least two nucleic acid molecules are the same.

382. The method of claim 368 wherein expression of the amino acid segment is induced.

383. The method of claim 296 wherein each nucleic acid molecule further comprises replication sequences, wherein the replication sequences mediate replication of the nucleic acid molecules.

384. The method of claim 383 wherein the nucleic acid molecules are replicated in vitro.

385. The method of claim 383 wherein the nucleic acid molecules are replicated in vivo.

386. The method of claim 385 wherein the nucleic acid molecules are replicated in cell culture.

387. The method of claim 296 wherein each nucleic acid molecule further comprises integration sequences, wherein the integration sequences mediate integration of the nucleic acid molecules into other nucleic acids.

388. The method of claim 387 wherein the nucleic acid molecules are integrated into a chromosome.

389. The method of claim 388 wherein the nucleic acid molecules are integrated into a chromosome at a predetermined location.

390. The method of claim 296 wherein the nucleic acids molecules are produced by replicating nucleic acids in one or more nucleic acid samples.

391. The method of claim 390 wherein the nucleic acids are replicated using pairs of primers, wherein each of the first primers in the primer pairs used to produce the nucleic acid molecules comprises a nucleotide sequence encoding the reporter signal peptide.

392. The method of claim 391 wherein each first primer further comprises expression sequences.

393. The method of claim 392 wherein the nucleotide sequence of each first primer also encodes an epitope tag.

394. The method of claim 296 wherein each amino acid segment further comprises an epitope tag.

395. The method of claim 394 wherein the epitope tag of each amino acid segment is different.

396. The method of claim 394 wherein the epitope tag of each amino acid segment is the same.

397. The method of claim 394 wherein the epitope tag of at least two amino acid segments are different.

398. The method of claim 394 wherein the epitope tag of at least two amino acid segments are the same.

399. The method of claim 394 wherein the amino acid segments are distinguished or separated from the one or more expression samples via the epitope tags.

400. The method of claim 296 wherein the reporter signal peptide of each amino acid segment is different.

401. The method of claim 296 wherein the reporter signal peptide of each amino acid segment is the same.

402. The method of claim 296 wherein the reporter signal peptide of at least two amino acid segments are different.

403. The method of claim 296 wherein the reporter signal peptide of at least two amino acid segments are the same.

404. The method of claim 296 wherein the nucleic acid molecules are in cells.

405. The method of claim 404 wherein each nucleic acid molecule is in a different cell.

406. The method of claim 404 wherein each nucleic acid molecule is in the same cell.

407. The method of claim 406 wherein each nucleic acid molecule further comprises expression sequences, wherein the expression sequences are operably linked to the nucleotide segment such that the amino acid segment can be expressed.

408. The method of claim 407 wherein the expression sequences of each nucleic acid molecule are different.

409. The method of claim 408 wherein the expression sequences are similarly regulated.

410. The method of claim 409 wherein a plurality of the expression sequences are expression sequences of, or derived from, genes expressed as part of the same expression cascade.

411. The method of claim 404 wherein the nucleic acid molecules are integrated into a chromosome of the cell.

412. The method of claim 411 wherein the nucleic acid molecules are integrated into the chromosome at a predetermined location.

413. The method of claim 411 wherein the chromosome is an artificial chromosome.

414. The method of claim 404 wherein the nucleic acid molecules are, or are integrated into, a plasmid.

415. The method of claim 404 wherein the cells are in cell lines.



416. The method of claim 415 wherein each nucleic acid molecule is in a different cell line.

417. The method of claim 415 wherein each nucleic acid molecule is in the same cell line.

418. The method of claim 404 wherein the expression samples are produced from the cells.

419. The method of claim 418 wherein each expression sample is produced from cells from a cell sample, wherein each expression sample is produced from a different cell sample.

420. The method of claim 419 wherein each cell sample is subjected to different conditions.

421. The method of claim 420 wherein each cell sample is brought into contact with a different test compound.

422. The method of claim 420 wherein each cell sample is cultured under different conditions.

423. The method of claim 420 wherein each cell sample is derived from a different organism.

424. The method of claim 420 wherein each cell sample is derived from a different tissue.

425. The method of claim 420 wherein each cell sample is taken from the same source at different times.

426. The method of claim 418 wherein the expression samples are produced by lysing the cells.

427. The method of claim 296 wherein the nucleic acid molecules are in organisms.

428. The method of claim 427 wherein each nucleic acid molecule is in a different organism.

429. The method of claim 427 wherein each nucleic acid molecule is in the same organism.

430. The method of claim 429 wherein each nucleic acid molecule further comprises expression sequences, wherein the expression sequences are operably linked to the nucleotide segment such that the amino acid segment can be expressed.

431. The method of claim 430 wherein the expression sequences of each nucleic acid molecule are different.

432. The method of claim 431 wherein the expression sequences are similarly regulated.

433. The method of claim 432 wherein a plurality of the expression sequences are expression sequences of, or derived from, genes expressed as part of the same expression cascade.

434. The method of claim 427 wherein the nucleic acid molecules are integrated into a chromosome of the organism.

435. The method of claim 434 wherein the nucleic acid molecules are integrated into the chromosome at a predetermined location.

436. The method of claim 434 wherein the chromosome is an artificial chromosome.

437. The method of claim 427 wherein the nucleic acid molecules are, or are integrated into, a plasmid.

438. The method of claim 427 wherein each nucleic acid molecule is in a different organism.

439. The method of claim 427 wherein each nucleic acid molecule is in the same organism.

440. The method of claim 296 wherein the nucleic acid molecules are in cells of an organism.

441. The method of claim 440 wherein the nucleic acid molecules are in substantially all of the cells of the organism.

442. The method of claim 440 wherein the nucleic acid molecules are in some of the cells of the organism.

443. The method of claim 440 wherein the amino acid segments are expressed in substantially all of the cells of the organism.

444. The method of claim 440 wherein the amino acid segments are expressed in some of the cells of the organism.

445. The method of claim 296 wherein the protein or peptide of interest of each amino acid segment is different.

446. The method of claim 296 wherein the protein or peptide of interest of each amino acid segment is the same.

447. The method of claim 296 wherein the protein or peptide of interest of at least two amino acid segments are different.

448. The method of claim 296 wherein the protein or peptide of interest of at least two amino acid segments are the same.

449. The method of claim 445 wherein the proteins or peptides of interest are related.

450. The method of claim 449 wherein the proteins or peptides of interest are proteins produced in the same cascade.

451. The method of claim 449 wherein the proteins or peptides of interest are proteins expressed under the same conditions.

452. The method of claim 449 wherein the proteins or peptides of interest are proteins associated with the same disease.

453. The method of claim 449 wherein the proteins or peptides of interest are proteins associated with the same cell type.

454. The method of claim 449 wherein the proteins or peptides of interest are proteins associated with the same tissue type.

455. The method of claim 449 wherein the proteins or peptides of interest are proteins in the same enzymatic pathway.

456. The method of claim 296 wherein the nucleotide segment encodes a plurality of amino acid segments each comprising a reporter signal peptide and a protein or peptide of interest.

457. The method of claim 456 wherein the protein or peptide of interest of at least two of the amino acid segments in one of the nucleotide segments are different.

458. The method of claim 456 wherein the protein or peptide of interest of the amino acid segments in one of the nucleotide segments are different.

459. The method of claim 456 wherein the protein or peptide of interest of at least two of the amino acid segments in each of the nucleotide segments are different.

460. The method of claim 456 wherein the protein or peptide of interest of the amino acid segments in each of the nucleotide segments are different.

461. The method of claim 456 wherein the set consists of a single nucleic acid molecule.

462. The method of claim 296 wherein the set consists of a single nucleic acid molecule, wherein the nucleic acid molecule comprises a plurality of nucleotide segments each encoding an amino acid segment.

463. The method of claim 296 wherein the amino acid segment comprises a cleavage site near the junction between the reporter signal peptide and the protein or peptide of interest.

464. The method of claim 463 wherein the cleavage site is cleaved.

465. The method of claim 464 wherein the reporter signal peptide is distinguished or separated from the peptide or protein of interest.

466. The method of claim 463 wherein the cleavage site is a trypsin cleavage site.

467. The method of claim 463 wherein the cleavage site is at the junction between the reporter signal peptide and the protein or peptide of interest.

468. The method of claim 296 wherein each amino acid segment further comprises a self-cleaving segment.

469. The method of claim 468 wherein the self-cleaving segment is between the reporter signal peptide and the protein or peptide of interest.

470. The method of claim 469 wherein the self-cleaving segment cleaves the amino acid segment.

471. The method of claim 470 wherein the reporter signal peptide is distinguished or separated from the peptide or protein of interest.

472. The method of claim 468 wherein the self-cleaving segment is an intein segment.

473. The method of claim 296 wherein a plurality of different altered reporter signal peptides are detected, wherein detection of each altered reporter signal peptide indicates expression of the amino acid segment that comprises the reporter signal peptide from which that altered reporter signal peptide is derived.

474. The method of claim 473 wherein different expression samples comprise different nucleic acid molecules, wherein detection of each altered reporter signal peptide indicates expression in the expression sample that comprises the nucleic acid

molecule that comprises the nucleotide segment encoding the amino acid segment that comprises the reporter signal peptide from which that altered reporter signal peptide is derived.

475. The method of claim 296 wherein there are a plurality of different expression samples, wherein each different expression sample comprises different nucleic acid molecules, wherein detection of an altered reporter signal peptide indicates expression in the expression sample that comprises the nucleic acid molecule that comprises the nucleotide segment encoding the amino acid segment that comprises the reporter signal peptide from which the detected altered reporter signal peptide is derived.

476. A method of detecting expression, the method comprising  
detecting a target altered reporter signal peptide derived from one or more expression samples,

wherein the one or more expression samples collectively comprise a set of nucleic acid molecules, wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides, wherein the target altered reporter signal peptide is one of the altered reporter signal peptides,

wherein detection of the target altered reporter signal peptide indicates expression of the nucleotide segment encoding the amino acid segment that comprises the reporter signal peptide from which the target altered reporter signal peptide is derived.

477. The method of claim 476 further comprising determining the amount of the target altered reporter signal peptide detected,

wherein the amount of the target altered reporter signal peptide indicates the amount present in the one or more expression samples of the nucleotide segment that

comprises the reporter signal peptide from which the target altered reporter signal peptide is derived.

478. The method of claim 477 wherein the amount of the nucleotide segment present is proportional to the amount of the target altered reporter signal peptide detected.

479. The method of claim 476 further comprising detecting a plurality of the altered reporter signal peptides,

wherein detection of each altered reporter signal peptide indicates expression of the nucleotide segment that comprises the reporter signal peptide from which that altered reporter signal peptide is derived.

480. The method of claim 479 further comprising determining the amount of the altered reporter signal peptides detected,

wherein the amount of each altered reporter signal peptide indicates the amount present in the one or more expression samples of the nucleotide segment that comprises the reporter signal peptide from which that altered reporter signal peptide is derived.

481. The method of claim 480 wherein the amount of the nucleotide segment present is proportional to the amount of the altered reporter signal peptide detected.

482. A method of detecting expression, the method comprising detecting a target altered amino acid segment derived from one or more expression samples,

wherein the one or more expression samples collectively comprise a set of nucleic acid molecules, wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the amino acid segments have a common property, wherein the common property allows the amino acid segments to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein alteration of the reporter signal peptides alters the amino acid segments, wherein the altered form of each amino acid segment can be distinguished from the altered forms of the other amino acid segments, wherein the target altered amino acid segment is one of the altered amino acid segments,

wherein detection of the target altered amino acid segment indicates expression of the amino acid segment from which the target altered amino acid segment is derived.

483. A method of detecting expression, the method comprising detecting an altered amino acid subsegment derived from one or more expression samples,

wherein the one or more expression samples collectively comprise a set of nucleic acid molecules, wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the amino acid segments each comprise an amino acid subsegment, wherein each amino acid subsegment comprises a portion of the protein or peptide of interest and all or a portion of the reporter signal peptide,

wherein the amino acid subsegments have a common property, wherein the common property allows the amino acid subsegments to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein alteration of the reporter signal peptides alters the amino acid subsegments, wherein the altered form of each amino acid subsegment can be distinguished from the altered forms of the other amino acid subsegments, wherein the target altered amino acid subsegment is one of the altered amino acid subsegments,

wherein detection of the target altered amino acid subsegment indicates expression of the amino acid segment from which the target altered amino acid subsegment is derived.

484. A method of detecting cells, the method comprising detecting a target altered reporter signal peptide derived from one or more cells, wherein the one or more cells collectively comprise a set of nucleic acid molecules, wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides, wherein the target altered reporter signal peptide is one of the altered reporter signal peptides,

wherein detection of the target altered reporter signal peptide indicates the presence of the cell from which the target altered reporter signal peptide is derived.

485. The method of claim 484 wherein each cell is engineered to contain at least one of the nucleic acid molecules, wherein the reporter signal peptide of the amino acid segment encoded by the nucleotide segment of the nucleic acid molecule in each cell is different.

486. The method of claim 485 wherein each cell having a trait of interest comprises the same reporter signal peptide.

487. The method of claim 486 wherein the trait of interest is a heterologous gene.

488. The method of claim 487 wherein the heterologous gene comprises the nucleic acid molecule.

489. The method of claim 486 wherein the heterologous gene encodes the amino acid segment.

490. The method of claim 484 wherein a plurality of different altered reporter signal peptides are detected, wherein detection of each altered reporter signal peptide indicates the presence of the cell from which that altered reporter signal peptide is derived.

491. The method of claim 490 wherein different cells comprise different nucleic acid molecules, wherein detection of each altered reporter signal peptide indicates the presence of the cell that comprises the nucleic acid molecule that comprises the nucleotide segment encoding the amino acid segment that comprises the reporter signal peptide from which that altered reporter signal peptide is derived.

492. The method of claim 484 wherein there are a plurality of different cells, wherein each different cell comprises different nucleic acid molecules, wherein detection of an altered reporter signal peptide indicates the presence of the cell that comprises the nucleic acid molecule that comprises the nucleotide segment encoding



the amino acid segment that comprises the reporter signal peptide from which the detected altered reporter signal peptide is derived.

493. A method of detecting cell samples, the method comprising detecting a target altered reporter signal peptide derived from one or more cell samples,

wherein the one or more cell samples collectively comprise a set of nucleic acid molecules, wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides, wherein the target altered reporter signal peptide is one of the altered reporter signal peptides,

wherein detection of the target altered reporter signal peptide indicates the presence of the cell sample from which the target altered reporter signal peptide is derived.

494. The method of claim 493 wherein a plurality of different altered reporter signal peptides are detected, wherein detection of each altered reporter signal peptide indicates the presence of the cell sample from which that altered reporter signal peptide is derived.

495. The method of claim 493 wherein different cell samples comprise different nucleic acid molecules, wherein detection of each altered reporter signal peptide indicates the presence of the cell sample that comprises the nucleic acid molecule that comprises the nucleotide segment encoding the amino acid segment that comprises the reporter signal peptide from which that altered reporter signal peptide is derived.

496. The method of claim 493 wherein there are a plurality of different cell samples, wherein each different cell sample comprises different nucleic acid molecules, wherein detection of an altered reporter signal peptide indicates the presence of the cell

sample that comprises the nucleic acid molecule that comprises the nucleotide segment encoding the amino acid segment that comprises the reporter signal peptide from which the detected altered reporter signal peptide is derived.

497. A method of detecting cells, the method comprising  
detecting a target altered reporter signal peptide derived from one or more cells,  
wherein the one or more cells collectively comprise a set of nucleic acid  
molecules, wherein each nucleic acid molecule comprises a nucleotide segment  
encoding an amino acid segment comprising a reporter signal peptide and a protein or  
peptide of interest,

wherein the reporter signal peptides have a common property, wherein the  
common property allows the reporter signal peptides to be distinguished or separated  
from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of  
each reporter signal peptide can be distinguished from the altered forms of the other  
reporter signal peptides, wherein the target altered reporter signal peptide is one of the  
altered reporter signal peptides,

wherein detection of the target altered reporter signal peptide indicates the  
presence of the cell from which the target altered reporter signal peptide is derived.

498. A method of detecting cells, the method comprising  
detecting a target altered amino acid segment derived from one or more cells,  
wherein the one or more cells collectively comprise a set of nucleic acid  
molecules, wherein each nucleic acid molecule comprises a nucleotide segment  
encoding an amino acid segment comprising a reporter signal peptide and a protein or  
peptide of interest,

wherein the amino acid segments have a common property, wherein the  
common property allows the amino acid segments to be distinguished or separated from  
molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein alteration of the  
reporter signal peptides alters the amino acid segments, wherein the altered form of  
each amino acid segment can be distinguished from the altered forms of the other  
amino acid segments, wherein the target altered amino acid segment is one of the  
altered amino acid segments,

wherein detection of the target altered amino acid segment indicates the presence of the cell from which the target altered amino acid segment is derived.

499. A method of detecting cells, the method comprising detecting an altered amino acid subsegment derived from one or more cells, wherein the one or more cells collectively comprise a set of nucleic acid molecules, wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the amino acid segments each comprise an amino acid subsegment, wherein each amino acid subsegment comprises a portion of the protein or peptide of interest and all or a portion of the reporter signal peptide,

wherein the amino acid subsegments have a common property, wherein the common property allows the amino acid subsegments to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein alteration of the reporter signal peptides alters the amino acid subsegments, wherein the altered form of each amino acid subsegment can be distinguished from the altered forms of the other amino acid subsegments, wherein the target altered amino acid subsegment is one of the altered amino acid subsegments,

wherein detection of the target altered amino acid subsegment indicates the presence of the cell from which the target altered amino acid subsegment is derived.

500. A method of detecting organisms, the method comprising detecting a target altered reporter signal peptide derived from one or more organisms,

wherein the one or more organisms collectively comprise a set of nucleic acid molecules, wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides, wherein the target altered reporter signal peptide is one of the altered reporter signal peptides,

wherein detection of the target altered reporter signal peptide indicates the presence of the organism from which the target altered reporter signal peptide is derived.

501. The method of claim 500 wherein each organism is engineered to contain at least one of the nucleic acid molecules, wherein the reporter signal peptide of the amino acid segment encoded by the nucleotide segment of the nucleic acid molecule in each organism is different.

502. The method of claim 501 wherein each organism having a trait of interest comprises the same reporter signal peptide.

503. The method of claim 502 wherein the trait of interest is a transgene.

504. The method of claim 503 wherein the transgene gene comprises the nucleic acid molecule.

505. The method of claim 502 wherein the transgene gene encodes the amino acid segment.

506. The method of claim 500 wherein a plurality of different altered reporter signal peptides are detected, wherein detection of each altered reporter signal peptide indicates the presence of the organism from which that altered reporter signal peptide is derived.

507. The method of claim 506 wherein different organisms comprise different nucleic acid molecules, wherein detection of each altered reporter signal peptide indicates the presence of the organism that comprises the nucleic acid molecule that comprises the nucleotide segment encoding the amino acid segment that comprises the reporter signal peptide from which that altered reporter signal peptide is derived.

508. The method of claim 500 wherein there are a plurality of different organisms, wherein each different organism comprises different nucleic acid molecules, wherein detection of an altered reporter signal peptide indicates the presence of the organism that comprises the nucleic acid molecule that comprises the nucleotide

segment encoding the amino acid segment that comprises the reporter signal peptide from which the detected altered reporter signal peptide is derived.

509. A method of detecting organisms, the method comprising detecting a target altered reporter signal peptide derived from one or more organisms,

wherein the one or more organisms collectively comprise a set of nucleic acid molecules, wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the reporter signal peptides have a common property, wherein the common property allows the reporter signal peptides to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein the altered form of each reporter signal peptide can be distinguished from the altered forms of the other reporter signal peptides, wherein the target altered reporter signal peptide is one of the altered reporter signal peptides,

wherein detection of the target altered reporter signal peptide indicates the presence of the organism from which the target altered reporter signal peptide is derived.

510. A method of detecting organisms, the method comprising detecting a target altered amino acid segment derived from one or more organisms,

wherein the one or more organisms collectively comprise a set of nucleic acid molecules, wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the amino acid segments have a common property, wherein the common property allows the amino acid segments to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein alteration of the reporter signal peptides alters the amino acid segments, wherein the altered form of each amino acid segment can be distinguished from the altered forms of the other

amino acid segments, wherein the target altered amino acid segment is one of the altered amino acid segments,

wherein detection of the target altered amino acid segment indicates the presence of the organism from which the target altered amino acid segment is derived.

511. A method of detecting organisms, the method comprising detecting an altered amino acid subsegment derived from one or more organisms,

wherein the one or more organisms collectively comprise a set of nucleic acid molecules, wherein each nucleic acid molecule comprises a nucleotide segment encoding an amino acid segment comprising a reporter signal peptide and a protein or peptide of interest,

wherein the amino acid segments each comprise an amino acid subsegment, wherein each amino acid subsegment comprises a portion of the protein or peptide of interest and all or a portion of the reporter signal peptide,

wherein the amino acid subsegments have a common property, wherein the common property allows the amino acid subsegments to be distinguished or separated from molecules lacking the common property,

wherein the reporter signal peptides can be altered, wherein alteration of the reporter signal peptides alters the amino acid subsegments, wherein the altered form of each amino acid subsegment can be distinguished from the altered forms of the other amino acid subsegments, wherein the target altered amino acid subsegment is one of the altered amino acid subsegments,

wherein detection of the target altered amino acid subsegment indicates the presence of the organism from which the target altered amino acid subsegment is derived.

512. A method comprising

(a) associating one of a plurality of reporter signals with one or more analytes in each of a plurality of samples,

wherein each reporter signal has a common property, wherein the common property allows each reporter signal to be separated from molecules lacking the common property,

(b) separating the analytes contained in each sample,

- (c) altering the reporter signals, and
- (d) detecting the altered forms the reporter signals.

513. The method of claim 512 further comprising, following step (a) and prior to step (b), combining two or more of the samples.

514. The method of claim 512 wherein analytes in each sample are associated with only one reporter signal, wherein the reporter signal associated with analytes in each sample is different.

515. The method of claim 512 wherein the analytes are separated by contact with a capture array.

516. A method comprising

(a) associating one of a plurality of coding tags with one or more analytes in at least one sample,

(b) separating the analytes contained in each sample;

(c) associating the coding tags with one or more reporter molecules, wherein each reporter molecule comprises a reporter signal and a decoding tag,

wherein each reporter signal has a common property, wherein the common property allows each reporter signal to be separated from molecules lacking the common property,

wherein each decoding tag is specific for one or more of the coding tags,

(d) altering the reporter signals, and

(e) detecting the altered forms the reporter signals.

517. The method of claim 516 wherein the coding tags are oligonucleotides, wherein the decoding tags are peptide nucleic acids, and wherein the reporter signals are reporter signal peptides.

518. A method comprising

(a) associating one of a plurality of coding tags with one or more analytes in at least one sample,

(b) separating the analytes contained in each sample;

(c) associating the coding tags with one or more reporter signals,

wherein each reporter signal has a common property, wherein the common property allows each reporter signal to be separated from molecules lacking the common property,

wherein each reporter signal is specific for one or more of the coding tags,

(d) altering the reporter signals, and

(e) detecting the altered forms the reporter signals.

519. The method of claim 518 wherein the coding tags are oligonucleotides, and wherein the reporter signals are peptide nucleic acids.

520. A method comprising

(a) associating one of a plurality of reporter signals with one or more analytes in each of a plurality of samples to form reporter signal/analyte conjugates,

wherein each reporter signal/analyte conjugate has a common property, wherein the common property allows each reporter signal/analyte conjugate to be separated from molecules lacking the common property,

(b) separating the analytes contained in each sample, wherein separation is not based on the common property of the reporter signal/analyte conjugates,

(c) altering the reporter signals thereby altering the reporter signal/analyte conjugates, and

(d) detecting the altered forms the reporter signal/analyte conjugates.

521. A method comprising

(a) associating one of a plurality of coding tags with one or more analytes in at least one sample,

(b) separating the analytes contained in each sample;

(c) associating the coding tags with one or more reporter molecules, wherein each reporter molecule comprises a reporter signal and a decoding tag,

wherein each reporter molecule has a common property, wherein the common property allows each reporter molecule to be separated from molecules lacking the common property,

wherein each decoding tag is specific for one or more of the coding tags,

(d) altering the reporter signals thereby altering the reporter molecules, and

(e) detecting the altered forms the reporter molecules.